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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/587,678

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EXAMINER

ORWIG, KEVIN S

ART UNIT

PAPER NUMBER

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/587,678	<b>Applicant(s)</b> UHRICH ET AL.	
	<b>Examiner</b> Kevin S. Orwig	<b>Art Unit</b> 1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 19 August 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,2,8-23,88,240 and 241 is/are pending in the application.
- 4a) Of the above claim(s) 88 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,8-23,240 and 241 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>8/19/19</u> .   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

The amendments and arguments filed Aug. 19, 2009 are acknowledged and have been fully considered. Claims 1, 2, 8-23, 88, 240, and 241 are now pending. Claims 3-7, 24-87, and 89-239 are cancelled; claim 23 is amended; claim 88 is withdrawn. Claims 1, 2, 8-23, 240, and 241 are now under consideration.

### ***OBJECTIONS/REJECTIONS WITHDRAWN***

The rejection of claim 23 under 35 U.S.C. 112, 2<sup>nd</sup> par. is withdrawn, in light of the claim amendments.

### ***OBJECTIONS/REJECTIONS MAINTAINED***

The rejection of claims 1, 2, 8-23, 240 and 241 under 35 U.S.C. 103(a) over TIAN and UHRICH is maintained as discussed below.

### ***Claim Rejections - 35 USC § 103 (Maintained)***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 1, 2, 8-23, 240 and 241 are rejected under 35 U.S.C. 103(a) as being unpatentable over TIAN (Tian *et al.* Polymer Preprints (2002) 43(2); 719-720) in view of UHRICH (WO 03/005959; Published Jan. 23, 2003; 2<sup>nd</sup> reference on IDS dated Nov. 17, 2006) (hereinafter '959).**

1. Tian discloses amphiphilic molecules of the structure depicted in formula III of instant claim 22 (elected species) that form stable polymeric micelles (p. 719, left col., 2<sup>nd</sup> par.; Scheme 1; 1<sup>st</sup> par. of Results and Discussion section). Tian teaches that these molecules are intermediates in the preparation of amphiphilic star-like macromolecules

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(ASMs) (2<sup>nd</sup> par. of Introduction). Tian teaches that these micelles have hydrophobic cores suitable as “microcontainers” for lipophilic compounds and that the hydrophilic/lipophilic ratios (HLB) can be controlled by changing the length of the PEG or acyl chains (first pars. of Introduction and Results and Discussion sections). Tian teaches that the micelles form 20 nm diameter aggregations (i.e. nanoparticulates).

2. While Tian discloses the molecules of applicants' elected species, and suggests that they have utility for the encapsulation of hydrophobic compounds, Tian does not explicitly teach the use of these compounds to remove low-density lipoproteins (LDL) or to treat atherosclerosis. Since Tian does not specifically disclose what types of molecules may be encapsulated within the micelles, one would be motivated to look to the related literature for guidance regarding such usage.

3. Uhrich discloses polymeric compounds that form stable micelles in solution, wherein the micelles have a hydrophobic core and act as microcontainers for lipophilic compounds (abstract; 1<sup>st</sup> par. on p. 2). Like the molecules of Tian, the hydrophobicity of Uhrich's compounds can be controlled by changing the length of the PEG or acyl chains (2<sup>nd</sup> par. on p. 34). Uhrich teaches that these micelles are particularly useful for solubilizing hydrophobic molecules (p. 26, 1<sup>st</sup> par.; and p. 34, last par.). Uhrich teaches the use of these compounds to sequester lipoproteins such as LDL that contribute to atherosclerosis (page 10, 4<sup>th</sup> par., elements (a) and (c)) by administering them to a patient in need of reducing the concentration of lipoproteins (p. 10, end of 4<sup>th</sup> par.). Uhrich teaches that such administration can minimize cardiovascular diseases, such as

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atherosclerosis, caused by the presence of excess LDL in the blood (p. 10, end of 4<sup>th</sup> par.).

4. Uhrich discloses embodiments of the compounds wherein they may contain the molecules taught by Tian (i.e. the instantly claimed molecules) as a part of their structure. For example, see Scheme 2 (top of p. 26), which discloses non-PEGylated versions of the instantly claimed molecules. It is noted that Uhrich teaches the use of polyethylene glycol (i.e. PEGylation) with these molecules (p. 29, 2<sup>nd</sup> par.). Additionally, Figure 10 teaches an embodiment wherein four of Tian's molecules are incorporated into a polyol core, the only difference from Tian's compounds being that the embodiment depicted in the figure contains an amide instead of an ester linkage between the mucic acid moiety and the mPEG moiety. It is noted that replacement of this amide by an ester is taught in Uhrich's disclosure (see description of the compounds on pages 2-8, particularly embodiment d) on p. 7, and the description of R<sup>4</sup> in this embodiment on p. 8). Thus, consistent with Tian's teaching, Tian's molecules are intermediates in the ASMs of Uhrich.

5. Given the similarity of the micelles formed by each of these molecules, and their identical intended uses to encapsulate hydrophobic compounds, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to utilize the molecules of Tian to treat atherosclerosis by sequestering or removing LDL as taught by Uhrich. One would have been motivated to do so since Tian suggests that the molecules are suitable for use with hydrophobic compounds, but does not teach which specific compounds are suitable. Thus, the ordinary artisan would have readily

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envisioned the use of Tian's intermediates in the same manner as the macromolecular ASMs of Uhrich. Further, the artisan would be motivated to use Tian's molecules since they are simpler than those of Uhrich and therefore would be easier and cheaper to prepare. The similarity of the micelles and use of both Tian's intermediates and Uhrich's ASMs would have provided the artisan with a high expectation that Tian's molecules would function in a substantially similar way and be useful in the treatment of atherosclerosis by sequestering LDL in the hydrophobic core. This is especially true given the direct teachings of both Tian and Uhrich that micelles of each of the disclosed compounds function in the same way, namely forming aggregates suitable to carry lipophilic compounds. Thus, claims 1, 2, 8-23, 240, and 241 are obvious over Tian and Uhrich.

Regarding the obviousness rejections herein, it is noted that a reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, in the absence of evidence to the contrary, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

### ***Response to Arguments***

Applicants' arguments have been fully considered but are not persuasive. Applicants argue that Tian does not specifically disclose the use of the disclosed compounds for LDL removal or treatment of atherosclerosis (response, p. 6).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Uhrich provides the teaching and suggestion to use the compounds for the removal of LDL and/or the treatment of atherosclerosis.

Applicants argue that the compounds of Uhrich differ "significantly" from the compounds disclosed by Tian because they comprise a polyfunctional core to which amphiphilic molecules are attached, which core is lacking in Tian. Applicants disagree that the compounds of Uhrich are essentially polymeric forms of the compounds of the instant compounds. Applicants argue that a skilled artisan would not have a reasonable expectation of success in using Tian's molecules (response, p. 6).

The examiner disagrees with applicants' assertion that the molecules of Uhrich are significantly different from those of Tian. It is noted that the molecules of Tian are encompassed by the disclosure of Uhrich as stated in the prior Office Action. The amphiphilic molecules, which are attached to the small core emphasized by applicants, can be the *same* molecules as disclosed by Tian, according to Uhrich's disclosure. Applicants have provided absolutely no evidence to suggest or demonstrate that adding



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a small polyfunctional core to Tian's (much larger) molecules would change the activity of the appended molecules, particularly given Tian's direct teaching that the non-polymerized molecules function in the same way. In order for applicants' argument to be persuasive, applicants must demonstrate that the functional part (i.e. the LDL-sequestering portion) of the molecule is the small polyfunctional core, which applicants have not done. In fact, Tian's teachings suggest otherwise. There is nothing to suggest that the micelles of Tian would be unsuitable for the same uses as the polymerized versions those of Uhrich. Since Tian directly teaches that the non-polymerized molecules form micelles capable of transporting lipophilic compounds (just like those of Uhrich), a skilled artisan would understand that it is the amphiphilic portions (i.e. Tian's molecules) themselves that are responsible for the sequestration of the hydrophobic compounds (i.e. per Tian's Scheme 1) rather than a small polyfunctional core that is present merely to link several of the amphiphilic compounds together. One would clearly have a reasonable expectation of success in using Tian's molecules for the same purposes as those described for the polymerized versions of Uhrich. Applicants provide no evidence of any kind to support their assertion that Uhrich's molecules are not simply polymerized versions of Tian's molecules.

Applicants argue that there is no teaching or suggestion in Uhrich to indicate that removal of the polyfunctional core would result in a compound that would operate as instantly claimed (response, p. 7).

This argument is unpersuasive since Tian provides the exact teaching that applicants allege is lacking in Uhrich. In response to applicants' arguments against the

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references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Tian teaches that applicants' elected species is capable of forming micelles that transport lipophilic compounds. One would clearly have a reasonable expectation of success in using Tian's molecules for the same purposes as those described for the polymerized versions of Uhrich which, besides a small polyfunctional core, are identical to those of Tian and are taught to function in the same way. Applicants are reminded of MPEP 2143.02, which states that "Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976). Also, When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). A *prima facie* case of obviousness has clearly been established.

### ***Summary/Conclusion***

Claims 1, 2, 8-23, 240, and 241 are rejected; claims 3-7, 24-87, and 89-239 are cancelled.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### ***Contact Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin S. Orwig whose telephone number is (571)270-5869. The examiner can normally be reached Monday-Friday 7:00 am-4:00 pm (with alternate Fridays off). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached Monday-Friday 8:00 am-5:00 pm at (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kevin S Orwig/

/David J Blanchard/  
Primary Examiner, Art Unit 1643